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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,437	11/16/2001	Avi J. Ashkenazi	P2730P1C49	2360

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HELLER EHRMAN WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CO 94025-3506

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,437	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/28/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendments filed 11/16/01 and 9/03/02 have been entered.

Specification

The disclosure is objected to because of the following informalities:. on p. 548, line 19, "samples" should be "sample".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119-124, 126-128, 132, 133 and dependent claims 125, 129-131, 134-138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 132 and 133 are indefinite because the metes and bounds of the claims are not clear. For claim 132 it is not clear if hybridization under any condition is permissible, even the most permissive, allowing non-specific hybridization to occur. For claim 133, while the skilled artisan understands the general concept of hybridization under "stringent conditions", what specific conditions are intended by the use of the term "stringent" in the present claims is unknown. What conditions of stringency are used in any particular situation are determined by the specificity of hybridization desired by the practitioner. The instant specification presents examples but not a limiting definition of "stringent conditions" (p. 312, line 23, through p. 313, line 5). In this case, the desired specificity is unknown. "Stringent" carries a meaning of "constricted", implying that not all hybridization conditions are acceptable. If however, there is a structural relatedness (limitation) that is being defined by the conditions, then those conditions or range of conditions must be clear in the claim.

Claims 119-124, 126-128 and 132 are indefinite for reciting "extracellular domain". The protein identified as PRO290 is disclosed as an intracellular protein (p. 340, line 20). It is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed

protein comprises an "extracellular domain" (for example see claim 119, parts (c) and (d)) is indefinite, as the art does not recognize intracellular proteins as having such a domain. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain..."lacking its associated signal sequence" (claim 39, part (d), for example) is indefinite because a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-124, 126, 128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack written description on two counts. First, claims are drawn to, for example, a nucleic acid encoding the polypeptide of SEQ ID NO:33, lacking its associated signal sequence. It is not clear if PRO290 has a signal sequence or if it does, what that sequence is. The specification discloses PRO290 of SEQ ID NO:33, but no domains are disclosed. The specification says PRO290 is believed to be an intracellular protein (p. 349, line 20). While there is some relationship to intracellular proteins FAN and beige (p. 410, line 18), shared sequence identity is not high (less than 20%, see SEQUENCE COMPARISON US 5,952,223) so correspondence to structure is difficult to make. It does not appear Applicants were in possession of a nucleic acid specifically lacking (or specifically including) a signal sequence.

Second, the claims are drawn to a nucleic acid having at least 80%, 85%, 90%, 95% or 99% sequence identity to a nucleic acid encoding a polypeptide with a particular disclosed sequence or drawn to a nucleic acid that hybridizes to SEQ ID NO:32. The claims do not require that the nucleic acid or encoded polypeptide possess any particular biological activity, nor any

particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Which nucleic acids of the genus comprising the required sequence are part of the invention has not been set forth.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only a nucleic acid of SEQ ID NO:32 or encoding SEQ ID NO:33, but not the full breadth of the claims meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claims 119-128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid of SEQ ID NO:33, does not reasonably provide enablement for other nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nucleic acid of SEQ ID NO:33 encodes a protein called PRO290. It is shown to have the ability to be used for screening for squama cell-type carcinomas (SqCCa or AdenSqCCa) in lung tissue. On pages 550 (TABLE 9A), use of SEQ ID NO :33 as probe showed a ΔCt greater than one in 5/11 lung squama cell-type carcinomas. No adenocarinoma lung tissue without a squamous component was positive. However, such screening was conducted with the nucleic acid of SEQ ID NO:33. Detection is predicated on structural relationship of the nucleic acid probe to nucleic acid(s) in the tumor tissue. One skilled in the art would not predict that detection would have the required sensitivity if the probe sequence differed from SEQ ID NO:33 such as the sequence of a degenerate nucleic acid or a hybridizing nucleic acid.

The claims are broad, including nucleic acids encoding SEQ ID NO:32 (*i.e.*, degenerate sequences) and nucleic acids at least 80% identical to thereto. There is no functional limitation associated with the nucleic acid or encoded protein in the claims. There is no use for the nucleic acid of SEQ ID NO:32 aside from screening lung tumor tissue for squama cell-type carcinomas. There is no disclosed function associated with PRO290.

Applicant say that PRO290 is most related to FAN and beige proteins; however, shared identity is less than 20%, too low to extrapolate function from structure. Further, the function of these proteins was unclear in the prior art. The prior art does not provide sufficient information

to allow the skilled artisan to use PRO290 or the encoding nucleic acid without significant further research.

For these reasons which include breadth of the claims, lack of information on the relationship of structure to function of PRO290, paucity of information in the prior art, limited working example, and lack of guidance for use provided in the specification, it would require undue experimentation to use the claimed nucleic acid commensurate in scope with the claims.

Priority

Priority application 09/380,137 and earlier filed priority applications do *not* meet the requirements of 35 U.S.C. § 112, first paragraph. While the sequence of PRO290 is disclosed, there was no function/use known to be associated with PRO290, and the skilled artisan would not have known how to use it. Therefore, the prior application also does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120. Note that even if priority were granted to the earliest filed priority application 60/092,472, the art rejection with US 6,607,879 below would remain under 35 UCS 102(e).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 119-121 and 132-134 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,607,879.

US 6,607,879 teaches the nucleic acid of SEQ ID NO:827 that is at least 99% identical (after introducing a gap) to SEQ ID NO:32 of the instant application because identity as defined in the specification is calculated can apparently be calculated relative to either sequence and is calculated after gaps are introduced to maximize matching nucleic acids. See attached SEQUENCE COMPARISON US 6,607,879.

Claims 119-121 and 132-134 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,952,223.

US 5,952,223 teaches the nucleic acid of SEQ ID NO:1 that would hybridize to SEQ ID NO:33 of the instant application and is at least 10 nucleotides in length. See attached SEQUENCE COMPARISON US 5,952,223.

Claims 119-121 and 132-135 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank AB011112.1.

GenBank AB011112.1 teaches a nucleic acid at least 99% identical to SEQ ID NO:32 of the instant application and which encodes a protein at least 99% identical to SEQ ID NO:33. See attached SEQUENCE COMPARISON GenBank AB011112.1. The nucleic acid was in a pBluescriptII SK plus vector (source).

Conclusion

Claims 129-131 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571)272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

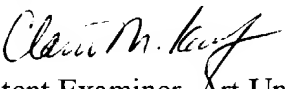
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571)272-0871.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or

applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.

5 

Patent Examiner, Art Unit 1646

April 15, 2004